

Solid-State Conformation of Copolymers of β -Benzyl-L-Aspartate with L-Alanine, L-Leucine, L-Valine, γ -Benzyl-L-Glutamate, or ϵ -Carbobenzoxy-L-Lysine

WILLEM L. SEDEREL,* ADRIAAN BANTJES, and JAN FEIJEN,[†]
*Department of Chemical Technology, Twente University of
Technology, Enschede, The Netherlands;* and JAMES M.
ANDERSON, *Macromolecular Science Division, Case Western Reserve
University, Cleveland, Ohio*

Synopsis

The solid-state conformation of copolymers of β -benzyl-L-aspartate [L-Asp(OBzl)] with L-leucine (L-Leu), L-alanine (L-Ala), L-valine (L-Val), γ -benzyl-L-glutamate [L-Glu(OBzl)], or ϵ -carbobenzoxy-L-lysine (Cbz-L-Lys) has been studied by ir spectroscopy and circular dichroism (CD). The ir spectra in the region of the amide I and II bands and in the region of 700–250 cm^{-1} have been determined. The results from the ir studies are in good agreement with data obtained by CD experiments. Incorporation of the amino acid residues mentioned above into poly[L-Asp(OBzl)] induces a change from the left-handed into the right-handed α -helix. This conformational change for the poly[L-Asp(OBzl)] copolymers was observed in the following composition ranges: L-Leu, 0–15 mol %; L-Ala, 0–32 mol %; L-Val, 0–8 mol %; L-Glu(OBzl), 3–10 mol %; and Cbz-L-Lys, 0–9 mol %.

INTRODUCTION

Polymers and copolymers of L-aspartic acid esters have been extensively investigated by means of conformational analyses, both experimentally and theoretically. The reason for this interest is the versatility of conformational behavior, in solution as well as in the solid state. Poly(β -benzyl-L-aspartate),^{1–3} poly[L-Asp(OBzl)], and poly(β -methyl-L-aspartate)^{3,4} were found to behave anomalously in that they adopt a left-handed α -helical conformation in chloroform solutions.

Malcolm⁵ has found that in the solid state, poly[L-Asp(OBzl)] is in the right-handed helical conformation when cast as monolayers on water from a dichloroacetic acid/chloroform (10–90%) solution. Exposure of dried films obtained from collapsed monolayers to the vapor of this solvent mixture results in a reverse transition from the right-handed to the left-handed form. Casting films from chloroform solution onto glass plates and allowing “normal” evaporation rates yields the left-handed α -helix.

* Present address: Royal Dutch Shell Laboratory, Amsterdam, The Netherlands.

[†] To whom correspondence should be addressed.

Heating these films to 140°C results in a different conformational transition⁶ from the α -helix to the ω -helix, which has also a left-handed sense. Another method of obtaining films of poly[L-Asp(OBzl)] in the left-handed ω -helix is by very slow evaporation from a chloroform solution.⁷ Heating films of poly[L-Asp(OBzl)] to 190°C results in a transition from the helical conformation to the β -sheet structure.⁷⁻⁹

Of special interest are the conformational studies of aspartate copolymers in which the two homopolymer components assume opposite helical senses. Copolymers of L-Asp(OBzl) with about 10 or more mol % of γ -benzyl-L-glutamate[L-Glu(OBzl)]^{1,2} have been shown to adopt the right-handed α -helix in chloroform solutions. Similar results were obtained for poly[L-Asp(OBzl)⁸⁰,L-Leu²⁰] and for poly[L-Asp(OBzl)⁸⁰,L-Ala²⁰].¹⁰

This paper deals with the conformation of copolymers of L-Asp(OBzl) and L-leucine (L-Leu), L-alanine (L-Ala), L-valine (L-Val), L-Glu(OBzl), or ϵ -carbobenzoxy-L-lysine (Cbz-L-Lys) in the solid state.

EXPERIMENTAL

The synthesis of the high-molecular-weight polypeptides has been reported elsewhere.¹¹ Only L- α -amino acids were used. All ir spectra were obtained on a Perkin Elmer model 521 spectrophotometer. Spectra of thin films of copolymers (2–15 μ m) cast from chloroform of chloroform/trifluoroacetic acid mixtures were recorded. Far-ir measurements were carried out in the Analytical Section of the Department of Chemical Technology Twente (Mr. L. Klop). CD measurements were recorded at 25°C in the 210–260-nm wavelength range using a Jasco J-20 recording spectrophotometer. Reproducible spectra of unoriented films cast in CD cells were obtained by using the method of Deshmane et al.¹² Very thin films (<2 μ m) were cast from dilute chloroform of chloroform/trifluoroacetic acid mixtures by slow evaporation of the solvent.

RESULTS

IR Spectroscopy: 1800–1500 cm^{-1}

A number of studies have shown the correlation between the conformations of poly(L-aspartic acid esters) and ir frequencies in the region of 1800–1500 cm^{-1} . A survey of the available data from the literature is given in Table I.^{3,9,13} It should be noted that the amide I frequencies for right-handed α -helix and random coil do not differ significantly, and in both cases the amide II absorption is usually rather broad. Therefore, discrimination between these two conformations is often difficult.

TABLE I
Infrared Frequencies (cm^{-1}) for Poly(β -Benzyl-L-Aspartates)

Conformation	Ester $\nu(\text{C}=\text{O})$	Amide I $\nu(\text{NHCO})$	Amide II $\delta(\text{NH}) + \nu(\text{N}-\text{C})$
Right-handed α -helix	1737	1658	1553
Left-handed α -helix	1737	1665	1558
ω -Helix	1731	1672	1536
β -Sheet	1732	1636	1535
Random coil (Ref. 14)	?	1655	1535

Copolymers of β -Benzyl-L-Aspartate with L-Leucine or L-Alanine

Table II shows the ir absorption data of films of poly[L-Asp(OBzl)], poly(L-Leu), poly(L-Ala), and their copolymers. Thin films of poly[L-Asp(OBzl)] cast from chloroform show the amide I adsorption at 1663 cm^{-1} and that of the amide II at 1555 cm^{-1} , consistent with the left-handed α -helix. Poly(L-Leu) shows the amide I and II absorptions at 1650 and 1545 cm^{-1} , respectively, indicative for a right-handed α -helix.¹⁴

Copolymers containing 15, 30, 50, and 67 mol % of L-Leu all show the amide I absorption in the vicinity of 1650 cm^{-1} and the amide II close to 1545 cm^{-1} . From these results it can be concluded that all copolymers of L-Asp(OBzl) and L-Leu are in the right-handed α -helix conformation.

The conformation of poly(L-Ala) depends to some extent on the solvent of polymerization.¹⁵ When films of poly(L-Ala) are cast from chloroform/trifluoroacetic acid, the spectra in the 1650-cm^{-1} region show that the polymer assumes the right-handed α -helical conformation.¹⁵ In the solid-state, copolymers of Ala with 35, 51, and 68 mol % of L-Asp(OBzl) show the features of the right-handed α -helical conformation.

TABLE II
Amide I and II Frequencies for Copolymers of β -Benzyl-L-Aspartate with L-Leucine or L-Alanine

Polymer Composition (mol %)	Frequency (cm^{-1})		Helix Sense
	Amide I	Amide II	
[Asp(OBzl)] _n	1663	1555	Left-handed
[Asp(OBzl) ⁶⁵ ,Leu ¹⁵] _n	1653	1549	Right-handed
[Asp(OBzl) ⁶⁵ ,Leu ³⁵] _n	1653	1548	Right-handed
[Asp(OBzl) ⁵⁰ ,Leu ⁵⁰] _n	1650	1546	Right-handed
[Asp(OBzl) ³³ ,Leu ⁶⁷] _n	1650	1546	Right-handed
(Leu) _n	1650	1545	Right-handed
[Asp(OBzl) ⁶⁸ ,Ala ³²] _n	1653	1547	Right-handed
[Asp(OBzl) ⁵¹ ,Ala ⁴⁹] _n	1652	1545	Right-handed
[Asp(OBzl) ³⁵ ,Ala ⁶⁵] _n	1653	1545	Right-handed
(Ala) _n	1656	1540	Right-handed

Copolymers of β -Benzyl-L-Aspartate with L-Valine

The spectra of films of poly[L-Asp(OBzl)] and poly(L-Val) together with their copolymers are shown in Fig. 1. As shown before, poly[L-Asp(OBzl)] is in the left-handed α -helix. Poly(L-Val) shows absorptions of the amide I and II at 1631 and 1534 cm^{-1} , indicative of the β -sheet structure.¹⁴ It is interesting to study the conformational aspects of their copolymers. In principle, the following conformations or mixtures thereof can be present: α -helix (either right- or left-handed), β -sheet, or random coil. Copolymers with 8, 16, and 32 mol % of L-Val have the amide I and II absorptions in the vicinity of 1650 and 1550 cm^{-1} . No absorptions indicative of the β -sheet conformation are observed. Far-ir spectroscopy and solid-state CD are necessary to discriminate between the existence of the right-handed α -helix and the random coil.

At high conversions the copolymerization of L-Asp(OBzl) NCA and L-Val NCA in methylene chloride/dioxane (3:1, v/v) yields large amounts of homopoly(L-Val).¹¹ Consequently, the ir spectrum of such a material shows a mixture of conformations, in which the β -sheet is present (absorptions at 1631 and 1534 cm^{-1}) in addition to the α -helix.

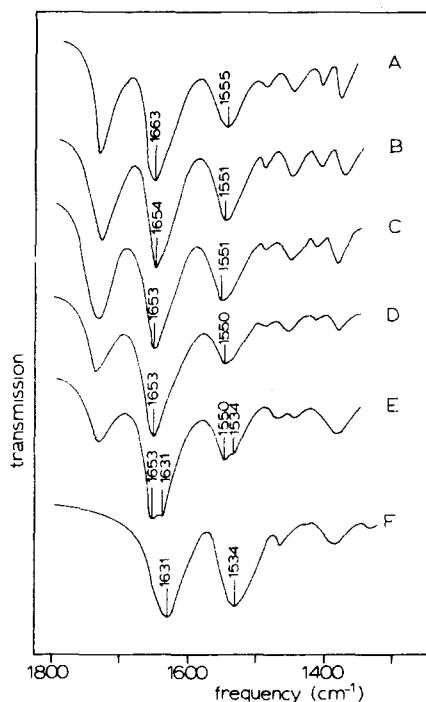


Fig. 1. The ir spectra of poly[L-Asp(OBzl),L-Val] with varying L-Asp(OBzl) contents (mol %): A, 100; B, 92; C, 84; D, 68; E, 51 (high conversion); and F, 0.

Copolymers of β -Benzyl-L-Aspartate with γ -Benzyl-L-Glutamate or ϵ -Carbobenzoxy-L-Lysine

Table III shows the amide I and II absorptions of films of poly[L-Asp(OBzl)], poly[L-Glu(OBzl)], poly(Cbz-L-Lys), and their copolymers. According to the observed frequencies, a copolymer of L-Asp(OBzl) with 3 mol % of L-Glu(OBzl) still has the left-handed α -helix.

Incorporation of 10 or more mol % of L-Glu(OBzl) causes a change in helix sense from the left-handed to the right-handed form.

An analogous situation is observed for copolymers of L-Asp(OBzl) and Cbz-L-Lys. Incorporation of 9 or more mol % of Cbz-L-Lys causes a change from the left-handed α -helix to the right-handed α -helix.

IR Spectroscopy: 800–250 cm^{-1}

The far-ir spectra of model compounds of polyglycine and polyalanines¹⁶ show that the bands in the region of 700–600 cm^{-1} are characteristic for the backbone conformation.

Itoh and coworkers studied copolymers of L-Ala with glycine or D-Ala¹⁵ and poly(α -amino acids) with alkyl side chains¹⁷ and their copolymers.¹⁸ Analysis of the spectra of poly(L-Val) with various degrees of polymerization has been reported by the same author.¹⁹ These studies were most encouraging, and the measurement of ir spectra in the region from 700 to 250 cm^{-1} was found to be a useful method of elucidating the conformation of these poly(α -amino acids).

TABLE III
Amide I and II Frequencies for Copolymers of β -Benzyl-L-Aspartate with γ -Benzyl-L-Glutamate or ϵ -Carbobenzoxy-L-Lysine

Polymer Composition (mol %)	Frequency (cm^{-1})		Helix Sense
	Amide I	Amide II	
[Asp(OBzl)] _n	1663	1555	Left-handed
[Asp(OBzl) ⁹⁷ , Glu(OBzl) ⁰³] _n	1662	1552	Left-handed
[Asp(OBzl) ⁹⁰ , Glu(OBzl) ¹⁰] _n	1653	1549	Right-handed
[Asp(OBzl) ⁸¹ , Glu(OBzl) ¹⁹] _n	1653	1549	Right-handed
[Asp(OBzl) ⁶⁴ , Glu(OBzl) ³⁶] _n	1651	1548	Right-handed
[Asp(OBzl) ⁴⁸ , Glu(OBzl) ⁵²] _n	1650	1548	Right-handed
[Glu(OBzl)] _n	1648	1546	Right-handed
[Asp(OBzl) ⁹¹ , Cbz-Lys ⁰⁹] _n	1652	1549	Right-handed
[Asp(OBzl) ⁸³ , Cbz-Lys ¹⁷] _n	1652	1549	Right-handed
[Asp(OBzl) ⁷⁰ , Cbz-Lys ³⁰] _n	1650	1548	Right-handed
[Asp(OBzl) ⁵⁰ , Cbz-Lys ⁵⁰] _n	1650	1547	Right-handed
[Asp(OBzl) ³⁰ , Cbz-Lys ⁷⁰] _n	1650	1544	Right-handed
[Cbz-Lys] _n	1649	1543	Right-handed

Copolymers of β -Benzyl-L-Aspartate and L-Leucine

Figure 2 shows the spectra of poly[L-Asp(OBzl)], poly(L-Leu), and their copolymers. There is a striking difference between the spectrum of poly[L-Asp(OBzl)] (A) and the copolymer with 15 mol % of L-Leu (B). Instead of the absorption at 455 cm^{-1} observed for poly[L-Asp(OBzl)], the copolymer shows three weaker absorptions at 490, 445, and 375 cm^{-1} with a shoulder at 395 cm^{-1} . Increasing the amount of L-Leu causes the two peaks at 490 and 445 cm^{-1} to coincide as one broader peak at 473 cm^{-1} , also present in poly(L-Leu). The peak at 375 cm^{-1} diminishes, and the initial shoulder at 395 cm^{-1} increases, in accordance with the findings of Itoh et al.¹⁸ for copolymers of L-Ala and L-Leu.

Itoh et al.¹⁷ concluded from analyses of the spectra of poly(L-Ala) (371-cm^{-1} band), poly(L- α -amino-*n*-butyric acid) (390-cm^{-1} band), poly(L-norvaline) (390-cm^{-1} band), poly(L-norleucine) (390-cm^{-1} band), and poly(L-Leu) (396-cm^{-1} band) that the band near 380 cm^{-1} is characteristic for the α -helix. As the band is absent in poly[L-Asp(OBzl)], which is known to be in the left-handed α -helix and present in all the [L-Asp(OBzl),L-Leu] copolymers, which are in the right-handed α -helix, it can be concluded that the band near 380 cm^{-1} is characteristic for the right-handed α -helix of poly(α -L-amino acids). Because this band is also present in poly(D-Ala), the conclusion is that this absorption is also characteristic for the left-handed α -helix of poly(α -D-amino acids).

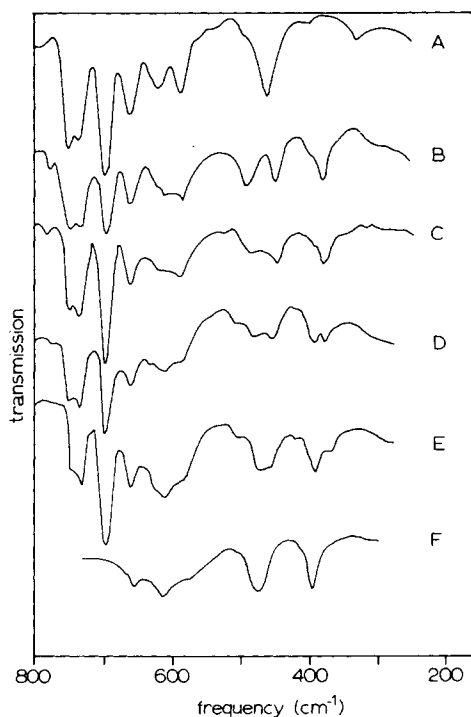


Fig. 2. The ir spectra of poly[L-Asp(OBzl),L-Leu] with varying L-Asp(OBzl) contents (mol %): A, 100; B, 85; C, 70; D, 50; E, 33; and F, 0.

Copolymers of β -Benzyl-L-Aspartate and L-Alanine

Figure 3 shows the spectra of poly[L-Asp(OBzl),L-Ala]. An absorption at 375 cm^{-1} is observed, indicating that the copolymers are present in the right-handed α -helix. Bands characteristic for L-Ala can be observed at 525 and 326 cm^{-1} , in accordance with data given by Itoh et al.¹⁷

Copolymers of β -Benzyl-L-Aspartate and γ -Benzyl-L-Glutamate

Figure 4(A)–(E) illustrates again the change in helix sense, which occurs when L-Glu(OBzl) is incorporated in poly[L-Asp(OBzl)]. Apparently, 3 mol % of L-Glu(OBzl) is not sufficient to induce this change: the ir spectrum is identical with that of poly[L-Asp(OBzl)]. For 10 or more mol % of L-Glu(OBzl), one observes the absorptions at 490 , 445 , and 375 cm^{-1} , which indicates that the copolymers are present in the right-handed α -helix. In the copolymer with 52 mol % of L-Glu(OBzl), one observes an additional absorption, at 406 cm^{-1} . An absorption at 409 cm^{-1} has been reported for poly[L-Glu(OBzl)] and for random copolymers of D- and L-Glu(OBzl) prepared by strong base²⁰ initiation. This absorption is said to be characteristic for the local α -helix of L-Glu(OBzl).¹⁴ The absorption is absent in copolymers of D- and L-Glu(OBzl) prepared by initiation with primary amines. Instead, two absorptions, one at 420 cm^{-1} and one at 402 cm^{-1} , are observed. These are believed to be due to L-units incorporated into a left-handed α -helix and D-units incorporated into a right-handed α -helix, respectively.²¹ Apparently, most L-Glu(OBzl) units in the copolymer with 52 mol % of L-Glu(OBzl) are in the right-handed α -helix.

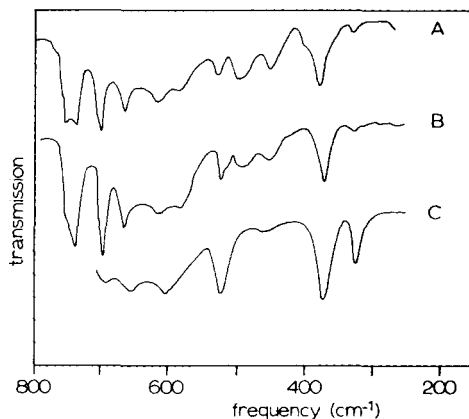


Fig. 3. The ir spectra of poly[L-Asp(OBzl),L-Ala] with varying Asp(OBzl) contents (mol %): A, 68; B, 51; and C, 0.

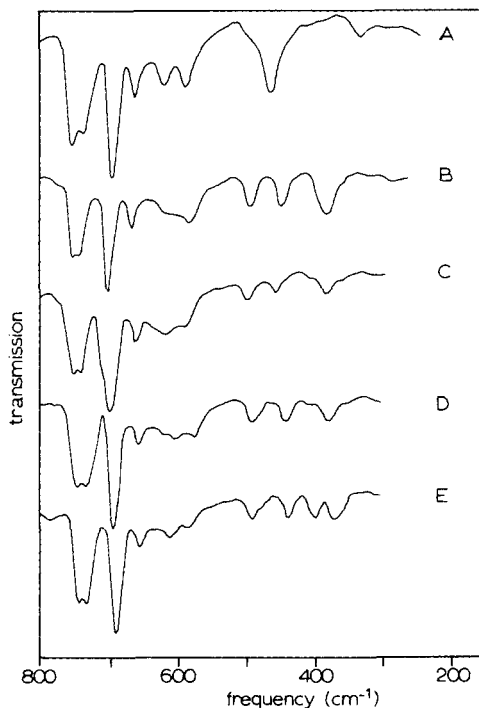


Fig. 4. The ir spectra of poly[L-Asp(OBzl),L-Glu(OBzl)] with varying L-Asp(OBzl) contents (mol %): A, 97; B, 90; C, 81; D, 64; and E, 48.

Copolymers of β -Benzyl-L-Aspartate and ϵ -Carbobenzoxy-L-Lysine

Incorporation of 9 or more mol % of Cbz-L-Lys into poly[L-Asp(OBzl)] induces a change in helix sense, as is apparent from the earlier observed bands at 490, 445, and 377 cm^{-1} . Even the copolymer containing 50 mol % of Cbz-L-Lys does not show an additional band characteristic for this unit.

Copolymers of β -Benzyl-L-Aspartate and L-Valine

The spectra of poly(L-Val) are dependent on the degree of polymerization and ir preparations technique, i.e., nujol mulls or films. High-molecular-weight poly(L-Val) ($DP = 600$) cast from trifluoroacetic acid exhibits absorption bands at 478, 437, and 324 cm^{-1} , in accordance with data obtained by Itoh and Fasman.¹⁹ From these data it can be concluded that the films are in the β -sheet conformation. Incorporation of small amounts of L-Val into the left-handed α -helix of poly[L-Asp(OBzl)] results in a change of helix sense, as is apparent from the absorptions at 490, 445, and 375 cm^{-1} (Fig. 5).

The material polymerized to high conversion, which is known to be heterogeneous,¹¹ shows different features in the ir spectrum. A broad band at about 718 cm^{-1} (amide V),¹⁹ together with small bands at 475 and 435 cm^{-1} , is indicative of the β -conformation. The small band at 375 cm^{-1}

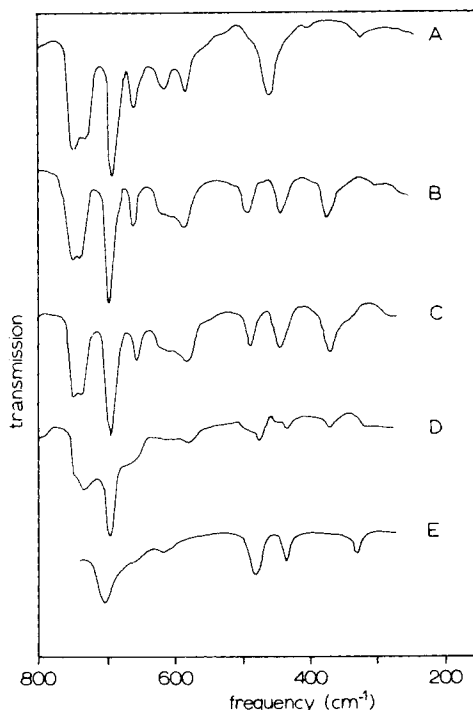


Fig. 5. The ir spectra of poly[L-Asp(OBzl),L-Val] with varying L-Asp(OBzl) contents (mol %): A, 100; B, 90; C, 82; D, 51 (high conversion); and E, 0.

shows that the right-handed α -helical conformation is also present in this material.

Circular Dichroism

There has been an interest in the CD spectra of polypeptide films, and in many cases identical spectra with those measured in solutions are obtained. However, if the material is strongly birefringent and/or oriented, additional complexities can result.²² Deshmane and coworkers¹² developed a method of obtaining reproducible spectra of unoriented films on CD cells, cast from dilute solution (0.1%) by slow evaporation of the solvent. Using the homopolymers as a reference, a good qualitative conformational analysis can be carried out for the aspartate copolymers.

Poly[L-Asp(OBzl)] exhibits a maximum at 226 nm, indicative of the left-handed α -helix. The homopolymers of L-Glu(OBzl), Cbz-L-Lys, L-Leu, and L-Ala all exhibit a minimum in the vicinity of 227 nm. This is a slightly higher value than the one observed in helicogenic solvents such as dioxane and tetrahydrofuran, where the $n - \pi^*$ transition usually occurs at 222 nm. Poly(L-Val) shows a minimum at 217–218 nm, a characteristic wavelength for the β -sheet, which has also been observed in solution.^{23,24}

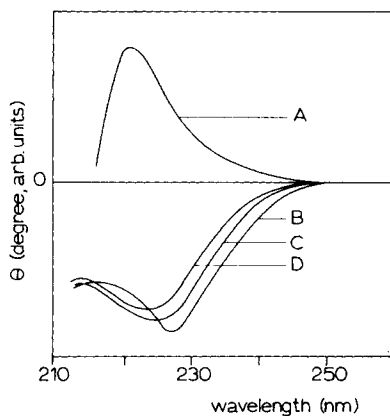


Fig. 6. The CD spectra (solid state) of poly[L-Asp(OBzl),L-Glu(OBzl)] with varying L-Asp(OBzl) contents (mol %): A, 97; B, 90; C, 81; and D, 48.

β-Benzyl-L-Aspartate Copolymers

The CD spectra of copolymers of L-Asp(OBzl) with L-Leu, L-Ala, or Cbz-L-Lys all exhibit a minimum in the vicinity of 225 nm, implying that they are all in the right-handed α -helix. CD spectra of [L-Asp(OBzl),L-Glu(OBzl)] copolymers (Fig. 6) show that the copolymer with 3 mol % of L-Glu(OBzl) is still in the left-handed α -helix (maximum at 222 nm). Incorporation of 10 or more mol % of L-Glu(OBzl) induces a change in helix sense, as is apparent from the observed minima at about 225 nm.

Figure 7 demonstrates the influence of incorporation of 8 (B), 16 (C), and 32 (D) mol % of L-Val in poly[L-Asp(OBzl)]. The observed curves (B), (C), and (D) are clearly different from the homopolymers (A) and (E), and their minima at 225 nm reveal that they are in the right-handed α -helix.

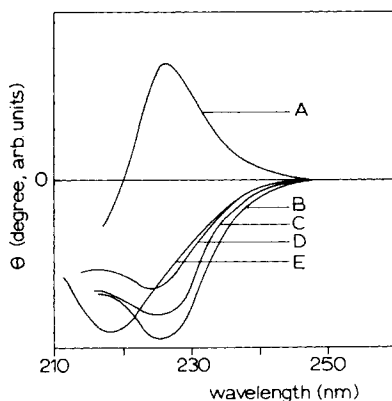


Fig. 7. CD spectra (solid state) of poly[L-Asp(OBzl),L-Val] with varying L-Asp(OBzl) contents (mol %): A, 100; B, 92; C, 84; D, 68; and E, 0.

DISCUSSION

The conformational analyses of the L-Asp(OBzl) copolymers studied by ir in the regions of 1800–1500 and 800–250 cm^{-1} and by solid-state CD are in good agreement. Especially the features observed in the far-ir and CD are clear-cut and unequivocal. It is of interest to note that the far-ir spectra of L-Asp(OBzl) copolymers with 15 mol % L-Leu, 10 mol % Glu(OBzl), 9 mol % Cbz-L-Lys, or 8 mol % L-Val are almost identical and characteristic for the right-handed α -helix of poly[L-Asp(OBzl)].

The effect of reversal of the helix sense of poly(α -amino acids) by incorporation of selected residues has been defined by Klug and Applequist²⁵ as conformational induction. They studied block copolypeptides of the type A_nB_m , in which B_m was D- or L-Glu(OBzl) and A_n a different amino acid which induced an opposite helix sense (conformational induction). Due to the well-defined sequence, they were able to study the effect of the AB-junction on conformational induction. Although the detailed side-chain geometry is difficult to predict, the location of the β -carbon atoms can be predicted from the known structure of the α -helix. When residue i is an A and residues $i + 3$ and $i + 4$ B's (the nearest-neighbors to residue i), the $C_i^\beta - C_{i+3}^\beta$ and $C_i^\beta - C_{i+4}^\beta$ distances will depend on both the helix sense and the amino acid configurations. These distances have been used to estimate the tendency toward interaction among side chains. Calculations for [L-Asp(OBzl) $_n$ -L-Glu(OBzl) $_m$] show that close contacts of the side chains are not involved in the induction of helix sense.

Conformational energy calculations have been carried out mainly by Scheraga and coworkers.^{26,27} They tried to explain the relative stability of right- and left-handed helical conformations as a function of the nature of the side chain. Two types of preferential conformations of the side chain have been found for each type of α -helix. (Comparison of the lowest energy conformation with the experimentally found helical sense shows agreement for most of the side chains.) The balance of forces is so delicate that small changes in the side-chain conformation could reverse the helix sense, which was predicted. It can be concluded from our study that introduction of small amounts of different amino acids into the aspartate helix does change this balance.

The effect of reversal in helix sense by incorporation of a β -former is very interesting. Our studies show that this reversal takes place when 8, 16, and 32 mol % L-Val are incorporated in the left-handed α -helix of L-Asp(OBzl). No β -structure has been observed in these polymers. They exhibit the right-handed α -helical conformation.

A similar observation has been reported for copolymers of L-Ala and L-Val, in which the L-Val residues are present in the α -helical conformation for contents up to 48 mol %.²⁸ Epand and Scheraga²⁴ have demonstrated the existence of the α -helical form of poly(L-Val) in solution under favorable conditions. This confirmed the theoretical predictions of Ooi et al.²⁶

Fraser studied sequential polypeptides of the [L-Glu(OMe) $_x$ -L-Val $_y$] $_n$ type and showed that their conformation was dependent on the position

of the valyl residues in the chain.²⁹ Since the α -helix has approximately 3.6 residues per turn, one would expect that valyl residues placed in the $i, i + 3$, and $i, i + 4$ positions would interact sterically, thus destabilizing the helix. For the homopolymer $[\text{Glu}(\text{OMe})_3]_n$, Fraser found a maximum helical content of about 60% in the solid state by ir spectroscopy. Introducing 20 mol % L-Val in position $i, i + 5$ of $[\text{L-Glu}(\text{OMe})_3\text{-L-Val-L-Glu}(\text{OMe})]_n$ only slightly decreased this content. When 25 mol % of L-Val is introduced in positions $i, i + 4$ of $[\text{L-Glu}(\text{OMe})_2\text{-L-Val-L-Glu}(\text{OMe})]_n$, the helix content was almost reduced by half, as was the case for 33 mol % L-Val in positions $i, i + 3$ in $[\text{L-Glu}(\text{OMe})\text{-L-Val-L-Glu}(\text{OMe})]_n$. However, if the polyhexapeptide $[\text{L-Glu}(\text{OMe})_3\text{-L-Val}_2\text{-L-Glu}(\text{OMe})]_n$ is examined (33 mol % L-Val), there is an increase in helicity to about 40%. The valyl residues in this polymer are positioned as $i, i + 1, i + 6, i + 7$, etc.

Returning to the $[\text{L-Asp}(\text{OBzl}), \text{L-Val}]$ copolymers, it was shown that these copolymers are almost ideally random.¹¹ Therefore, fractions of the valyl residues in $i, i + 3$ and $i, i + 4$ will be present, and we expect that these polymers will have a decreased helical content.

References

1. Bradbury, E. M., Downie, A. R., Elliot, A. & Hanby, W. E. (1960) *Proc. R. Soc. London, Ser. A* **259**, 110–128.
2. Karlson, R. H., Norland, K. S., Fasman, G. D. & Blout, E. R. (1960) *J. Am. Chem. Soc.* **82**, 2268–2275.
3. Bradbury, E. M., Carpenter, B. G. & Goldman, H. (1968) *Biopolymers*, **6**, 837–850.
4. Goodman, M., Boardman, F. & Litowsky, I. (1963) *J. Am. Chem. Soc.* **85**, 2491–2497.
5. Malcolm, B. R. (1970) *Biopolymers* **9**, 911–922.
6. Bradbury, E. M., Brown, L., Downie, A. R., Elliott, A., Fraser, R. D. B. & Hanby, W. E. (1962) *J. Mol. Biol.* **5**, 230–247.
7. Obata H. & Kanetsuna, H. (1971) *J. Polym. Sci., Pt. A-2* **9**, 1977–1989.
8. Bradbury, E. M., Brown, L., Downie, A. R., Elliott, A., Fraser, R. D. B., Hanby, W. E. & McDonald, T. R. R. (1960) *J. Mol. Biol.* **2**, 276–286.
9. Green, D. B., Happey, F. & Watson, B. M. (1970) *Eur. Polym. J.* **6**, 7–16.
10. Bradbury, E. M., Carpenter, B. G., Crane-Robinson, C. & Goldman, H. (1972) *Macromolecules* **5**, 557–564.
11. Sederel, W. L. (1977) Thesis, Twente University of Technology, Department of Chemical Technology, Enschede, The Netherlands.
12. Deshmane, S. S., Hayashi, T., Sederel, W. L. & Anderson J. M. (1978) *Biopolymers* **17**, 2851–2864.
13. Frushour B. G. & Koenig, J. L. (1975) *Biopolymers* **14**, 2115–2135.
14. Miyazawa, T. (1967) *Poly(α -Amino Acids)*, Fasman, G. D., Ed., Dekker, New York, pp. 69–103.
15. Itoh, K., Nakahara, T., Shimanouchi, T., Oya, M., Uno, K. & Iwakura, Y. (1968) *Biopolymers* **6**, 1759–1766.
16. Koyama, Y. & Shimanouchi, T. (1968) *Biopolymers* **6**, 1037–1076.
17. Itoh, K., Shimanouchi, T. & Oya, M. (1969) *Biopolymers* **7**, 649–658.
18. Itoh, K., Oya, M. & Shimanouchi, T. (1972) *Biopolymers* **11**, 1137–1147.
19. Itoh, K. & Fasman, G. D. (1975) *Biopolymers* **14**, 1755–1767.
20. Akaïke, T., Inoue, S. & Itoh, K. (1974) *Biopolymers* **13**, 1713–1719.
21. Itoh, K., Ozaki, T., Nagayama, K., Wada, A. & Tsuboi, M. (1973) *Macromolecules* **6**, 654–656.

22. Stevens, L., Townend, R., Timasheff, S. N., Fasman, G. D. & Potter, J. (1968) *Biochemistry* **7**, 3717–3720.
23. Kubota, S. & Fasman, G. D. (1975) *Biopolymers* **14**, 605–631.
24. Epand, R. F. & Scheraga, H. A. (1968) *Biopolymers* **6**, 1551–1571.
25. Klug, T. L. & Applequist, J. (1974) *Biopolymers* **13**, 1317–1340.
26. Ooi, T., Scott, R. A., Vanderkooi, G. & Scheraga, H. A. (1967) *J. Chem. Phys.* **46**, 4410–4426.
27. Yan, J. F., Vanderkooi, G. & Scheraga, H. A. (1968) *J. Chem. Phys.* **49**, 2713–2726.
28. Itoh, K. & Katabuchi, H. (1973) *Biopolymers* **12**, 921–929.
29. Fraser, R. D. B., Harrap, B. S., McRae, T. P., Stewart, F. H. C. & Suzuki, E. (1965) *J. Mol. Biol.* **12**, 482–490.

Received July 23, 1979

Accepted April 4, 1980